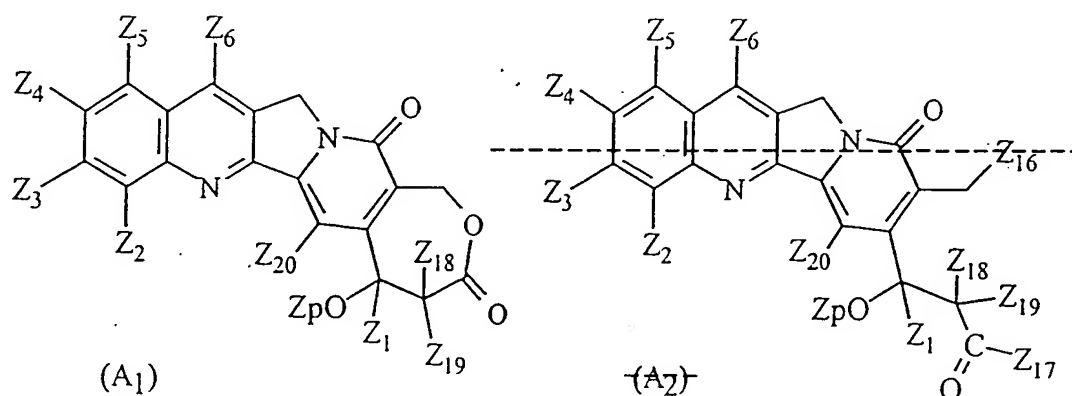


## AMENDMENTS TO THE CLAIMS

### Claim 1 (currently amended)

A compound of the formula



in racemic or enantiomeric form or any combination of these forms, wherein

$Z_1$  is a member selected from the group consisting of lower alkyl, lower alkenyl, lower alkynyl, lower haloalkyl, lower alkoxy lower alkyl and lower alkylthio lower alkyl;

$Z_2$ ,  $Z_3$ ,  $Z_4$ ,  $Z_5$  and  $Z_6$  are independently a member selected from the group consisting of,

- i) H, halo, lower haloalkyl, alkyl of 1 to 12 carbon atoms unsubstituted or substituted by at least one halo, lower alkenyl, cycloalkyl, cycloalkyl lower alkyl, cyano lower cyanoalkyl, nitro, lower nitroalkyl, amido, lower amidoalkyl, hydrazino, lower hydrazinoalkyl, azido, lower azidoalkyl, lower alkyl lower sulphonylalkyl,  $-(CH_2)_mNZ'_6Z'_7$ ,  $-(CH_2)_mOZ'_6$ ,

$-(CH_2)_mCO_2Z'_6$ ,  $-(CH_2)_mCO_2Z'_6$ ,  $-(CH_2)_mNZ'_6C(O)Z_8$ ,  $-(CH_2)_mC(O)Z_8$ ,  
 $-(CH_2)_mOC(O)Z_8$ ,  $-O-(CH_2)_mNZ'_6Z'_7$ ,  $-OC(O)NZ'_6Z'_7$ ,  $-OC(O)$   
 $(CH_2)_mCO_2Z'_6$ ,  $-OSO_2Z_7$ ,  $-(CH_2)_mN(CH_3)_nNZ'_6Z'_7$ , -  
 $(CH_2)_mOC(O)NZ'_6Z'_7$ ,  $-(CH_2)_mS(O)_qZ_{11}$ ,  $-(CH_2)_mP(O)Z_{12}Z_{13}$ , -  
 $(CH_2)_2P(S)Z_{12}Z_{13}$ ,  $-(CH_2)_mSiZ'_{11}Z'_{12}Z'_{13}$ ; or ii)  $-(CH_2)_n[N=X]$ , -  
 $OC(O)[N=X]$ ,  $-(CH_2)_mOC(O)[N=X]$ , aryl and lower arylalkyl, each  
unsubstituted or substituted with 1 to 4 members on the aryl or the  
heterocycle selected from the group consisting of lower alkyl, lower  
arylalkyl, halo, hydroxy,  $-OCF_3$ , nitro, amino, lower alkylamino, di(lower  
alkyl) amino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and  
lower alkoxy lower alkyl or iii)  $Z_3$  and  $Z_4$  or  $Z_4$  and  $Z_5$  form together a  
chain of 3 or 4 members in which the elements of the chain are selected  
from the group consisting of CH,  $CH_2$ , O, S, N or  $NZ_9$ ;

$Z_7$  is a member selected from the group consisting of lower alkyl  
unsubstituted or substituted by at least one halod, arylk, aryl unsubstituted  
or substituted by at least one lower alkyl;

$Z'_6$  and  $Z'_7$  are independently a member selected from the group consisting of i) H,  
lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower  
aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower  
alkoxy lower alkyl and haloalkyl, or ii) aryl or lower arylalkyl,  
unsubstituted or substituted on the aryl with 1 to 4 members selected from

the group consisting of lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl;

Z<sub>8</sub> is a member selected from the group consisting of i) H, lower alkyl, lower hydroxyalkyl, amino, lower alkylamino, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy, lower alkoxy lower alkyl and lower haloalkyl, or ii) aryl or lower arylalkyl unsubstituted or substituted on the aryl with 1 to 4 members selected from the group consisting of lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl ;

Z<sub>9</sub> is a member selected from the group consisting of i) H, lower alkyl, lower haloalkyl, or ii) aryl and lower arylalkyl unsubstituted or substituted with a member selected from the group consisting of lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl;

Z<sub>10</sub> is a member selected from the group consisting of i) H, lower alkyl, lower haloalkyl and lower alkoxy, or ii) aryl unsubstituted or substituted on the aryl with a member selected from the group consisting of lower alkyl, lower haloalkyl, lower hydroxyalkyl and lower alkoxy lower alkyl;

Z<sub>11</sub> is a member selected from the group consisting of lower alkyl, aryl,  $-(CH_2)_mOZ_{14}$ ,  $-(CH_2)_mSZ_{14}$ ,  $-(CH_2)_2NZ_{14}Z_{15}$  and  $(CH_2)_m[N=X]$ ;

- $Z_{12}$  and  $Z_{13}$  are independently members selected from the group consisting of lower alkyl, aryl, lower alkoxy, aryloxy and amino;
- $Z'_{11}$ ,  $Z'_{12}$  and  $Z'_{13}$  are independently a member selected from the group consisting of H or lower alkyl;
- $Z_{14}$  and  $Z_{15}$  are independently a member selected from the group consisting of H, lower alkyl and aryl;
- $Z_{16}$  is H or  ~~$OZ_{24}$~~ ;
- $Z_{17}$  is  ~~$OZ'_6$  or  $NZ'_6$  or  $NZ'_6Z'_7$~~ ;
- $Z_{18}$  and  $Z_{19}$  are independently a member selected from the group consisting of H, halo, lower alkyl, lower alkoxy and hydroxy;
- $Z_{20}$  is H or halo;
- $Z_{21}$  is ~~a member selected from the group consisting of H, lower alkyl, CHO and  $C(O)(CH_2)_mCH_3$~~ ;
- $Z_p$  is a member selected from the group consisting of H or an easily cleavable group preferably chosen from the groups corresponding to the formula  $-C(O)-A-NZ_{22}Z_{23}$  in which A represents a linear or branched alkylene unsubstituted or substituted by a member selected from the group consisting of free, esterified or salified hydroxy, halogen, free, esterified or salified carboxy, amino, mono and dialkylamino;
- $Z_{22}$  and  $Z_{23}$  are independently a member selected from the group consisting of i) H, lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower

aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or ii) aryl or lower arylalkyl unsubstituted or substituted on the aryl with 1 to 4 members selected from the group consisting of lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl;

m is an integer between 0 and 6;

n is 1 or 2; and

q is an integer from 0 to 2; and

[N=X] is a heterocyclic group with 4 to 7 ring members with the nitrogen atom which a member of the heterocyclic ring, and X is the chain necessary to complete said heterocyclic group and selected from the group consisting of O, S, CH<sub>2</sub>, CH, N, NZ<sub>9</sub> and C(O)Z<sub>10</sub>;

and or its pharmaceutically acceptable salt.

**Claim 2** (currently amended)

A compound of claim 1, in racemic or enantiomeric form or any combinations of these forms, wherein

$Z_1$  is a member selected from the group consisting of lower alkyl, lower alkenyl, lower alkynyl, lower haloalkyl, lower alkoxy lower alkyl and lower alkylthio lower alkyl;

$Z_2$  is a member selected from the group consisting of H, halo and  $-\text{OSO}_2Z_7$ ;

$Z_3$ ,  $Z_4$  and  $Z_5$  are independently a member selected from the group consisting of i) H, halo, lower haloalkyl, lower alkyl, lower alkenyl, cyano, lower cyanoalkyl, nitro, lower nitroalkyl, amido, lower amidoalkyl, hydrazino, lower hydrazinoalkyl, azido, lower azidoalkyl,  $-(\text{CH}_2)_m\text{NZ}'_6Z'_7$ ,  $-(\text{CH}_2)_m\text{OZ}'_6$ ,  $-(\text{CH}_2)_m\text{SZ}'_6$ ,  $-(\text{CH}_2)_m\text{CO}_2Z'_6$ ,  $-(\text{CH}_2)_m\text{NZ}'_6\text{C}(\text{O})Z_8$ ,  $-(\text{CH}_2)_m\text{C}(\text{O})Z_8$ ,  $-(\text{CH}_2)_m\text{OC}(\text{O})Z_8$ ,  $-\text{O}(\text{CH}_2)_m\text{NZ}'_6Z'_7$ ,  $-\text{OC}(\text{O})\text{NZ}'_6Z'_7$ ,  $-\text{OC}(\text{O})(\text{CH}_2)_m\text{CO}_2Z'_6$  and  $-\text{OSO}_2Z_7$  or ii)  $-(\text{CH}_2)_n[\text{N}=\text{X}]$ ,  $-\text{OC}(\text{O})[\text{N}=\text{X}]$ ,  $-(\text{CH}_2)_m\text{OC}(\text{O})[\text{N}=\text{X}]$  wherein  $[\text{N}=\text{X}]$  is a heterocyclic group with 4 to 7 ring members with the nitrogen atom, which is a member of the heterocyclic group, and X is the remaining members, which are necessary to complete the heterocyclic group, selected from the group consisting of O, S,

CH<sub>2</sub>, CH, N, NZ<sub>9</sub> and COZ<sub>10</sub>, aryl or lower arylalkyl, unsubstituted or substituted on the aryl or the heterocycle with 1 to 4 members selected from the group consisting of lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl or iii) Z<sub>3</sub> and Z<sub>4</sub> or Z<sub>4</sub> and Z<sub>5</sub> form together a chain with 3 or 4 members in which the elements of the chain are selected from the group consisting of CH, CH<sub>2</sub>, O, S, N and NZ<sub>9</sub>;

Z<sub>6</sub>

is a member selected from the group consisting of  
 i) H, halo, lower haloalkyl, alkyl containing 1 to 12 carbon atoms unsubstituted or substituted by at least one halo, lower alkoxy, lower alkoxy lower alkyl, lower alkylthio lower alkyl, cycloalkyl, cycloalkyl lower alkyl, cyano, cyanoalkyl, lower alkyl lower sulphonylalkyl, lower hydroxyalkyl, nitro,  $-(CH_2)_mC(O)Z_8$ ,  $-(CH_2)_mNZ'_6C(O)Z_8$ ,  
 $-(CH_2)_mNZ'_6Z'_7$ ,  $-(CH_2)_mN(CH_3)(CH_2)_nNZ'_6Z'_7$ ,  
 $-(CH_2)_mOC(O)Z_8$ ,  $-(CH_2)_mOC(O)NZ'_6Z'_7$ ,  $-(CH_2)_mS(O)_qZ_{11}$ ,  
 $-(CH_2)_mP(O)Z_{12}Z_{13}$ ,  $-(CH_2)_2P(S)Z_{12}Z_{13}$ , and  
 $-(CH_2)_mSiZ'_{11}Z'_{12}Z'_{13}$ ; or ii)  $-(CH_2)_n[N=X]$ ,  $-OC(O)[N=X]$ ,  
 $-(CH_2)_mOC(O)[N=X]$ , each unsubstituted or unsubstituted on the heteroaryl with 1 to 4 members of the group consisting of lower alkyl, lower

arylalkyl, halo, hydroxy, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl; or iii) aryl or lower arylalkyl, each unsubstituted or substituted on the aryl with 1 to 4 members of the group consisting of lower alkyl, halo, hydroxy, nitro,  $-OCF_3$ , amino, lower alkylamino, di(lower alkyl)amino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl;

$Z_7$  is a member selected from the group consisting of lower alkyl unsubstituted or substituted by at least one halo, or unsubstituted or substituted by at least one lower alkyl;

$Z'_6$  and  $Z'_7$  are independently a member selected from the group consisting of i) H, lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl and lower haloalkyl, or ii) aryl or lower arylalkyl unsubstituted or substituted on the aryl with 1 to 4 members of the group consisting of lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl;



Z<sub>8</sub>

is a member selected from the group consisting of  
i) H, lower alkyl, lower hydroxyalkyl, amino, lower  
alkylamino, lower alkyl lower aminoalkyl, lower  
aminoalkyl cycloalkyl, cycloalkyl lower alkyl,  
lower alkenyl, lower alkoxy, lower alkoxy lower  
alkyl and lower haloalkyl, or ii) aryl or lower  
arylalkyl unsubstituted or substituted on the aryl  
with 1 to 4 members of the group consisting of  
lower alkyl, halo, nitro, amino, lower alkylamino,  
lower haloalkyl, lower hydroxyalkyl, lower alkoxy  
and lower alkoxy lower alkyl;

Z<sub>9</sub>

is a member selected from the group consisting of  
i) H, lower alkyl and lower haloalkyl, or ii) aryl  
or lower arylalkyl, unsubstituted or substituted  
with a member of the group consisting of lower  
alkyl, halo, nitro, amino, lower alkylamino, lower  
haloalkyl, lower hydroxyalkyl, lower alkoxy and  
lower alkoxy lower alkyl;

Z<sub>10</sub>

is a member selected from the group consisting of  
i) H, lower alkyl, lower haloalkyl and lower  
alkoxy, or ii) aryl unsubstituted or substituted on  
the aryl with 1 to 4 members of the group  
consisting of lower alkyl, lower haloalkyl, lower  
hydroxyalkyl and lower alkoxy lower alkyl;

$Z_{11}$  is a member selected from the group consisting of lower alkyl, aryl,  $-(CH_2)_mOZ_{14}$ ,  $-(CH_2)_mSZ_{14}$ ,  $-(CH_2)_2NZ_{14}Z_{15}$  and  $-(CH_2)_m[N=X]$ ;

$Z_{12}$  and  $Z_{13}$  are independently a member selected from the group consisting of lower alkyl, aryl, lower alkoxy, aryloxy and amino;

$Z'_{11}$ ,  $Z'_{12}$  and  $Z'_{13}$  are independently H or lower alkyl;

$Z_{14}$  and  $Z_{15}$  are independently a member selected from the group consisting of H, lower alkyl and aryl;

~~$Z_{16}$  is H or  $-OZ_{21}$~~

~~$Z_{17}$  is  $-OZ'_{16}$  or  $-NZ'_{16}Z'_{17}$~~

$Z_{18}$  and  $Z_{19}$  are independently a member selected from the group consisting of H, halo, lower alkyl, lower alkoxy and hydroxy;

$Z_{20}$  is H or halo;

~~$Z_{21}$  is a member selected from the group consisting of H, lower alkyl,  $-CHO$  and  $-C(O)(CH_2)_mCH_3$ ;~~

$Z_p$  represents H or an easily cleavable group of the formula  $-C(O)-A-NZ_{22}Z_{23}$ , wherein A is alkylene unsubstituted or substituted by a member selected from the group consisting of free, esterified or salified hydroxy, halogen, free, esterified or salified carboxy, amino and mono and dialkylamino;

$Z_{22}$  and  $Z_{23}$  are independently a member selected from the group consisting of i) H, lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or ii) aryl or lower arylalkyl unsubstituted or substituted by 1 to 4 members of the group consisting of lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy and lower alkoxy lower alkyl;

m is an integer between 0 and 6; and

n is 1 or 2; and

q is an integer from 0 to 2; and

[N=X] is a heterocyclic group with 4 to 7 ring members

with the nitrogen atom which is a member of the heterocyclic ring, and X is the chain necessary to complete said heterocyclic group and is selected from the group consisting of O, S, CH<sub>2</sub>, CH, N, NZ<sub>9</sub> and COZ<sub>10</sub>;

~~and~~ or a pharmaceutically acceptable salt thereof;

**Claim 3** (currently amended)

A compound of claim 1 wherein Z<sub>2</sub> is H or halo ~~and~~ or a pharmaceutically acceptable salt thereof.

**Claim 4** (currently amended)

A compound of claim 1 wherein Z<sub>3</sub> is halo; ~~and~~ or a pharmaceutically acceptable salt thereof.

**Claim 5** (currently amended)

A compound of claim 1 wherein

Z<sub>1</sub> is lower alkyl;

Z<sub>2</sub> is H or halo;

Z<sub>3</sub> Z<sub>4</sub> and are independently a member selected from the group consisting of

i) H, halo, lower alkyl, -(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>Z'<sub>7</sub>, -(CH<sub>2</sub>)<sub>m</sub>OZ'<sub>6</sub> and -OSO<sub>2</sub>Z<sub>7</sub>

or

ii) -(CH<sub>2</sub>)<sub>n</sub>[N=X] or

iii) Z<sub>3</sub> and Z<sub>4</sub> or Z<sub>4</sub> and Z<sub>5</sub> form together a chain with 3 or 4 members in which the elements of the chain are selected from the group

consisting of CH, CH<sub>2</sub>, O, S, N and NZ<sub>9</sub>;

Z<sub>6</sub> is a member selected from the group consisting of  
i) H, halo, alkyl of 1 to 12 carbon atoms  
unsubstituted or substituted by at least one halo,  
lower alkoxy lower alkyl, cycloalkyl, cycloalkyl  
lower alkyl, lower hydroxyalkyl, -(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>Z'<sub>7</sub> and  
-(CH<sub>2</sub>)<sub>m</sub>SiZ'<sub>11</sub>Z'<sub>12</sub>Z'<sub>13</sub>; or ii) -(CH<sub>2</sub>)<sub>n</sub>[N=X] unsubstituted  
or substituted with lower alkyl or lower arylalkyl  
or iii) aryl or lower arylalkyl unsubstituted or  
substituted with a member selected from the group  
consisting of lower alkyl, halo, -OCF<sub>3</sub>, di(lower  
alkyl)amino and lower haloalkyl;

Z<sub>7</sub> is lower alkyl unsubstituted or substituted by at  
least one halo;

Z'<sub>6</sub> and Z'<sub>7</sub> are independently i) H, or lower alkyl, or ii)  
lower arylalkyl;

Z<sub>9</sub> is lower alkyl or lower arylalkyl;

Z'<sub>11</sub>, Z'<sub>12</sub> and Z'<sub>13</sub> are independently lower alkyl;

~~Z<sub>16</sub> is H or -OZ<sub>17</sub>-~~

~~Z<sub>17</sub> is -OZ'<sub>6</sub> or -NZ'<sub>6</sub>Z'<sub>7</sub>;~~

Z<sub>18</sub> and Z<sub>19</sub> are independently H or halo;

Z<sub>20</sub> is H;

~~Z<sub>21</sub> is a member selected from the group consisting of H, lower alkyl or -C(O)(CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub>;~~

Z<sub>p</sub> is H or -C(O)-A-N<sub>22</sub>Z<sub>23</sub>, in which A is alkylene unsubstituted or substituted by a member selected from the group consisting of free, esterified or salified hydroxy, halogen, free, esterified or salified carboxy, amino and mono and dialkylamino radicals;

Z<sub>22</sub> and Z<sub>23</sub> are independently H or lower alkyl;

m is an integer between 0 and 6;

n is 1 or 2; and

q is an integer from 0 to 2; and

[N=X] is a heterocyclic group with 4 to 7 ring members, X is the chain necessary to complete said

heterocyclic group and is selected from the group consisting of O, CH<sub>2</sub>,  
CH, N and NZ<sub>9</sub>;  
~~and~~ or a pharmaceutically acceptable salt thereof.

**Claim 6 (currently amended)**

A compound of claim 1 wherein Z<sub>18</sub>, Z<sub>19</sub> and Z<sub>20</sub> are H; ~~and~~ or a pharmaceutically acceptable salt thereof.

**Claim 7 (currently amended)**

A compound of claim 1 wherein Z<sub>1</sub> is ethyl ~~and~~ or a pharmaceutically acceptable salt thereof.

**Claim 8 (currently amended)**

A compound of claim 1 wherein Z<sub>p</sub> is -C(O)-A-NZ<sub>22</sub>Z<sub>23</sub> ~~and~~ or a pharmaceutically acceptable salt thereof.

**Claim 9 (currently amended)**

A compound of claim 1 wherein Z<sub>p</sub> is H ~~and~~ or a pharmaceutically acceptable salt thereof.

**Claims 10 and 11 (currently cancelled)**

**Claim 12** (currently amended)

A compound of claim 1 wherein  $Z_6$  is  $-(CH_2)_mSiZ'_{11}Z'_{12}Z'_{13}$  ~~and~~ or a pharmaceutically acceptable salt thereof.

**Claim 13** (amended)

A compound of claim 1 selected from the group consisting of:

(5R)-5-ethyl-9,10-difluoro-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4': 6,7] indolizino[1,2-b]quinoline-3,15-dione; and

(5R)-5-ethyl-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4': 6,7]indolizino[1,2-b]quinoline-3,15-dione.

**Claim 14** (currently amended)

A compound of claim 1 wherein  $Z_2$  is H or halo,  $Z_3$  is halo,  $Z_4$  is a member selected from the group consisting of H, halo and lower alkyl,  $Z_5$  is H or halo, and  $Z_6$  is a member selected from the group consisting of H, lower alkyl and  $-(CH_2)_n[N=X]$  substituted with lower alkyl ~~and~~ or a pharmaceutically acceptable salt thereof.



**Claim 15** (currently amended)

A compound of claim 1 selected from the group consisting of:

(5R)-5-ethyl-9,11-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxino[3',4' : 6,7]

indolizino[1,2-b]quinoline-3,15-dione; and

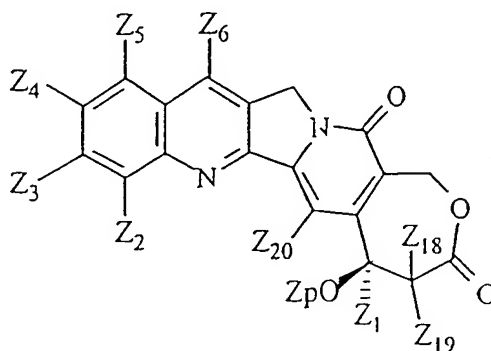
(5R)-5-ethyl-9,11-difluoro-5-hydroxy-12-propyl-4,5,13,15-tetrahydro-1H,3H-oxepino

[3',4' : 6,7]indolizino[1,2-b]quinoline-3,15-dione; ~~and~~ or a pharmaceutically acceptable

salt thereof.

**Claim 16** (currently amended)

A compound of claim 1 having the formula



wherein Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub>, Z<sub>6</sub>, Z<sub>18</sub>, Z<sub>19</sub>, Z<sub>20</sub> and Z<sub>p</sub> are as defined in claim 1 ~~and~~ or a pharmaceutically acceptable salt thereof.

**Claims 17 to 27 (currently cancelled)**